```
? ds

Set      Items   Description
S1      185265   RECEPTOR(5N)ACTIVAT?
S2      415056   CONFIGURATION
S3         673   S1 AND S2
S4     1153437   FIT? OR MATCH?
S5          13   S3 AND S4
S6          10   RD (unique items)
? s ligand(5n)configuration
          405349  LIGAND
          415056  CONFIGURATION
      S7     515  LIGAND(5N)CONFIGURATION
? s s1 and s7
          185265  S1
             515  S7
      S8       6  S1 AND S7
? rd
>>>Duplicate detection is not supported for File 340.

>>>Records from unsupported files will be retained in the RD set.
...completed examining records
      S9       3  RD (unique items)
? t s9/3,k,ab/1-3

 9/3,K,AB/1      (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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14083848   PMID: 11855982
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Secondary structure of the third extracellular loop responsible for ligand selectivity of a mammalian gonadotropin-releasing hormone receptor.

Petry Renate; Craik David; Haaima Gerald; Fromme Bernhard; Klump Horst; Kiefer Wolfgang; Palm Dieter; Millar Robert

Institut fur Physikalische Chemie, Universitat Wurzburg, Am Hubland, D-97074 Wurzburg, Germany.

Journal of medicinal chemistry (United States) Feb 28 2002, 45 (5) p1026-34, ISSN 0022-2623 Journal Code: 9716531

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

The extracellular loop 3 (ECL3) of the mammalian gonadotropin-releasing hormone receptor (GnRH-R) contains an acidic amino acid (Glu(301) in the mouse GnRH-R) that confers agonist selectivity for Arg(8) in mammalian GnRH. It is proposed that a specific conformation of ECL3 is necessary to orientate the carboxyl side chain of the acidic residue for interaction with Arg(8) of GnRH, which is supported by decreased affinity for Arg(8) GnRH but not Gln(8) GnRH when an adjacent Pro is mutated to Ala. To probe the structural contribution of the loop domain to the proposed presentation of the carboxyl side chain, we synthesized a model peptide (CGPEMLNRVSEPGC) representing residues 293-302 of mouse ECL3, where Cys and Gly residues are added symmetrically at the N and C termini, respectively, allowing the introduction of a disulfide bridge to simulate the distances at which the ECL3 is tethered to the transmembrane domains 6 and 7 of the receptor. The ability of the ECL3 peptide to bind GnRH with low affinity was demonstrated by its inhibition of GnRH stimulation of inositol phosphate production in cells expressing the GnRH-R. The CD bands of the ECL3 peptides exhibited a superposition of predominantly unordered structure and partial contributions from beta-sheet structure. Likewise, the analysis of the

amide I and amide III bands from micro-Raman and FT Raman experiments revealed mainly unordered conformations of the cyclic and of the linear peptide. NMR data demonstrated the presence of a beta-hairpin among an ensemble of largely disordered structures in the cyclic peptide. The location of the turn linking the two strands of the hairpin was assigned to the three central residues L(296), N(297), and R(298). A small population of structured species among an ensemble of predominantly random coil conformation suggests that the unliganded receptor represents a variety of structural conformers, some of which have the potential to make contacts with the ligand. We propose a mechanism of **receptor activation** whereby binding of the agonist to the inactive receptor state induces and stabilizes a particular structural state of the loop domain, leading to further conformational rearrangements across the transmembrane domain and signal propagating interaction with G proteins. Interaction of the Glu(301) of the receptor with Arg(8) of GnRH induces a folded **configuration** of the **ligand** . Our proposal thus suggests that conformational changes of both ligand and receptor result from this interaction.

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9/3,K,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12687750 PMID: 10607675
The structure, organization, activation **and plasticity of the erythropoietin** receptor .
Wilson I A; Jolliffe L K
Department of Molecular Biology, Skaggs Institute for Chemical Biology, The Scripps Research Institute, La Jolla 92037, USA. wilson@scripps.edu
Current opinion in structural biology (ENGLAND) Dec 1999, 9 (6) p696-704, ISSN 0959-440X Journal Code: 9107784
Contract/Grant No.: GM49497; GM; NIGMS
Publishing Model Print
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Dimerization of the erythropoietin receptor has long been accepted as the singular step in its mechanism of activation. Recent studies have revealed a regulator process for activation that is dependent on the actual **configuration** of the receptor- **ligand** dimer assembly. This aspect of the receptor subunit assembly appears to extend to the unliganded receptor, which can dimerize on the cell surface and diminish any spontaneous background signaling in the absence of ligand. This self-recognition, as well as the multiple ligand binding capabilities of the receptor binding site, is consistent with an emerging theme of plasticity in protein-protein and ligand-receptor interactions.

The structure, organization, activation **and plasticity of the erythropoietin** receptor .
... Recent studies have revealed a regulator process for activation that is dependent on the actual **configuration** of the receptor- **ligand** dimer

assembly. This aspect of the receptor subunit assembly appears to extend to the unliganded...

9/3,K,AB/3 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

13563569 Genuine Article#: 896NY Number of References: 30
Title: Estrogen stimulates release of secreted amyloid precursor protein from primary rat cortical neurons via protein kinase C pathway (ABSTRACT AVAILABLE)
Author(s): Zhang S; Huang Y; Zhu YC; Yao T (REPRINT)
Corporate Source: Fudan Univ,Shanghai Med Coll, Dept Physiol & Pathophysiol,Shanghai 200032//Peoples R China/ (REPRINT); Fudan Univ,Shanghai Med Coll, Dept Physiol & Pathophysiol,Shanghai 200032//Peoples R China/; Fudan Univ,Shanghai Med Coll, State Key Lab Med Neurobiol,Shanghai 200032//Peoples R China/(tyao@shmu.edu.cn)
Journal: ACTA PHARMACOLOGICA SINICA, 2005, V26, N2 (FEB), P171-176
ISSN: 1671-4083 Publication date: 20050200
Publisher: ACTA PHARMACOLOGICA SINICA, 294 TAI-YUAN ROAD, SHANGHAI 200031, PEOPLES R CHINA
Language: English Document Type: ARTICLE
Abstract: Aim: To investigate the mechanism of the action of estrogen, which stimulates the release of secreted amyloid precursor protein alpha (sAPPalpha) and decreases the generation of amyloid-beta protein (Abeta), a dominant component in senile plaques in the brains of Alzheimer's disease patients.

Methods: Experiments were carried out in primary rat cortical neurons, and Western blot was used to detect sAPPalpha in a culture medium and the total amount of cellular amyloid precursor protein (APP) in neurons.

Results: 17beta-Estradiol (but not 17alpha-estradiol) and beta-estradiol 6-(O-carboxymethyl) oxime: BSA increased the secretion of sAPPalpha and this effect was blocked by protein kinase C (PKC) inhibitor calphostin C, but not by the classical estrogen receptor antagonist ICI 182,780. Meanwhile, 17beta-estradiol did not alter the synthesis of cellular APP.

Conclusion: The effect of 17beta-estradiol on sAPPalpha secretion is likely mediated through the membrane binding sites, and needs molecular **configuration** specificity of the **ligand** . Furthermore, the action of the PKC-dependent pathway might be involved in estrogen-induced sAPPalpha secretion.

...Abstract: estradiol on sAPPalpha secretion is likely mediated through the membrane binding sites, and needs molecular **configuration** specificity of the **ligand** . Furthermore, the action of the PKC-dependent pathway might be involved in estrogen-induced sAPPalpha ...
...Identifiers--ALZHEIMERS-DISEASE; **RECEPTOR** -ALPHA; BETA PEPTIDES; NEUROPROTECTION; **ACTIVATION;** ESTRADIOL; MIDBRAIN; CASCADE; BRAIN; CELLS
?

The distinct agonistic properties of the phenylpyrazolosteroid cortivazol reveal interdomain communication within the glucocorticoid receptor.

Yoshikawa Noritada; Yamamoto Keiko; Shimizu Noriaki; Yamada Sachiko; Morimoto Chikao; Tanaka Hirotoshi

Division of the Clinical Immunology, the Advanced Clinical Research Center, the Institute of Medical Science, the University of Tokyo, 4-6-1 Shirokanedai, Minato-ku, Tokyo 108-8639, Japan.

Molecular endocrinology (Baltimore, Md.) (United States) May 2005, 19 (5) p1110-24, ISSN 0888-8809 Journal Code: 8801431

Publishing Model Print-Electronic

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: In Process

Recent structural analyses of the nuclear receptors establish a paradigm of **receptor activation** , in which agonist binding induces the ligand binding domain (LBD)/activation function-2 helix to form a charge clamp for coactivator recruitment. However, these analyses have not sufficiently addressed the mechanisms for differential actions of various synthetic steroids in terms of fine tuning of multiple functions of whole receptor molecules. In the present study, we used the glucocorticoid receptor (GR)-specific agonist cortivazol (CVZ) to probe the plasticity and functional modularity of the GR. Structural docking analysis revealed that although CVZ is more bulky than other agonists, it can be accommodated in the ligand binding pocket of the GR by reorientation of several amino acid side chains but without major alterations in the active conformation of the LBD. In this induced **fit** model, the phenylpyrazole A-ring of CVZ establishes additional contacts with helices 3 and 5 of the LBD that may contribute to a more stable LBD **configuration** . Structural and functional analysis revealed that CVZ is able to compensate for the deleterious effects of a C-terminal deletion of the LBD in a manner that mimics the stabilizing influence of the F602S point mutation. CVZ-mediated productive recruitment of transcriptional intermediary factor 2 to the C-terminally deleted LBD requires the receptor's own DNA binding domain and is positively influenced by the N-terminal regions of GR or progesterone receptor. These results support a model where ligand-dependent conformational changes in the LBD play a role in GR-mediated gene regulation via modular interaction with the DBD and activation function-1.

Recent structural analyses of the nuclear receptors establish a paradigm of **receptor activation** , in which agonist binding induces the ligand binding domain (LBD)/activation function-2 helix to...

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